MAR 2 2 2013

510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: K121946

Owners Name:

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Name of contact person:

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QA/RA Director
Axis-Shield Diagnostics Ltd.

Date summary prepared:

March 8th, 2013

Device Name: Axis-Shield Active-B12 (Holotranscobalamin)

Classification Name: Vitamin B12 test system

Trade Name: Axis-Shield Active-B12 (Holotranscobalamin)

Common Name: Holotranscobalamin test

Governing Regulation: 862.1810

Device Classification: Class II

Classification Panel: Clinical Chemistry

Product Code: CDD

Legally marketed device to which equivalency is claimed:

ARCHITECT Active-B12 (Holotranscobalamin) (K112443)

Intended Use of Device:

The Axis-Shield Active-B12 (Holotranscobalamin) assay is an enzyme-immunoassay (EIA) for the quantitative determination of holotranscobalamin (HoloTC) in human serum. HoloTC (vitamin B_{12} bound to transcobalamin) is used as an aid in the diagnosis and treatment of vitamin B_{12} deficiency.

Description of Device:

The Axis-Shield Active-B12 (Holotranscobalamin) device contains the following components: a microtitre plate with 8 x 12-well breakapart strips coated with a anti-holotranscobalamin murine monoclonal antibody, in a resealable foil pack with desiccant; ready-to-use calibrators, low and high controls (phosphate buffer containing protein (bovine) stabiliser and sodium azide preservative with or without recombinant HoloTC); ready-to-use pre-treatment solution; murine anti-human transcobalamin alkaline phosphatase conjugate; para-NitroPhenyl Phosphate (pNPP) substrate; wash buffer (8x); ready-to-use stop solution.

Principle of the Assay:

The microtitre wells are coated with a highly specific monoclonal antibody for Active-B12 (Holotranscobalamin). During the first incubation holotranscobalamin in serum specifically binds to the antibody-coated surface. In the second incubation the Conjugate binds to any captured holotranscobalamin. The wells are then washed to remove unbound components. Bound holotranscobalamin is detected by incubation with the Substrate. Addition of Stop Solution terminates the reaction, resulting in a coloured end-product. The concentration of holotranscobalamin in pmol/L is directly related to the colour generated and can be estimated by interpolation from a dose-response curve based on Calibrators.

Comparison of Technological Characteristics:

Axis-Shield Active-B12 (Holotranscobalamin) and ARCHITECT Active-B12 (Holotranscobalamin) are both immunoassays for the quantitative determination of Holotranscobalamin (HoloTC) in human serum.

The predicate device is an automated Chemiluminescent mircoparticle immunoassay (CMIA) whereas the submission device is a manual enzyme-linked immunosorbent assay. Both assays also demonstrated substantial equivalence in terms antibodies employed and units of measure.

Comparison of the subject device with the predicate device:

Parameter	Submission device Axis-Shield Active-B12 (Holotranscobalamin)	Predicate device
Intended use	The Axis-Shield Active-B12 (Holotranscobalamin) assay is an enzyme-immunoassay (EIA) for the quantitative determination of holotranscobalamin (HoloTC) in human serum. HoloTC (vitamin B12 bound to transcobalamin) is used as an aid in the diagnosis and treatment of vitamin B12 deficiency.	Chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of Holotranscobalamin in human serum on the ARCHITECT i System. Active-B12 (Holotranscobalamin) is used as an aid in the diagnosis and treatment of vitamin B12 deficiency.
Antibodies employed	Murine monoclonal antibody 3C4 Murine monoclonal antibody 3-11	Murine monoclonal antibody 3C4 Murine monoclonal antibody 3-11
Substrate / Signal Generation	Alkaline phosphatase	Acridinium Tracer
Specimen type	Serum and Serum Separator	Serum and Serum Separator
Storage conditions	2-8ºC.	2-8ºC.
Calibration	6-point calibration curve. Linear regression curve-fit	6-point calibration curve. 4PLC Y-weighted
Measuring Interval	10 to 128 pmol/L	5.0 to 128.0 pmol/L
Detection Limits	Limit of Quantitation of 8.3 pmol/L	Limit of Quantitation of ≤ 5.0 pmol/L
Linearity on Dilution	LOQ to Calibrator F	LOQ to Calibrator F
Expected Values in Asymptomatic Population	The mean Holotranscobalamin concentration (derived from log-transformed data to normalize the population) was 72 pmol/L with a range from 15 to 147 pmol/L. The central 95% of the population defined the expected range of 21 to 123pmol/L (n= 135)	The mean Holotranscobalamin concentration (derived from log-transformed data to normalize the population) was 71.9pmol/L with a range from 20.6 to 196.7 pmol/L. The central 95% of the population defined the expected range of 25.1 to 165.0 pmol/L (n=181)
Cross-reactivity	No detectable carryover with; Apotranscobalamin at 500 pmol/L Haptocorrin at 5000 pmol/L	No detectable carryover with; Apotranscobalamin at 500 pmol/L Haptocorrin at 5000 pmol/L
Interference	≤ 10% with; Bilirubin at 0.3 mg/mL Haemoglobin at 5 mg/mL Triglycerides at 30 mg/mL Rheumatoid Factor at 75 IU/mL Total protein at 90 mg/mL	≤ 10% with; Bilirubin at 20 mg/dL Haemoglobin at 200 mg/dL Triglycerides at 850 mg/dL Rheumatoid Factor at 70 IU/mL Total protein at 10 g/dL
Imprecision	Total %CV ≤ 12% Within-run %CV ≤ 9%	Total %CV ≤ 5.8% Within-run %CV ≤ 4.4%

Summary of Non-Clinical Performance:

The Axis-Shield Active-B12 (Holotranscobalamin) and ARCHITECT Active-B12 (Holotranscobalamin) are both immunoassays for the quantitative determination of Holotranscobalamin (HoloTC) in human serum.

The Axis-Shield Active-B12 (Holotranscobalamin) assay demonstrated substantially equivalent performance to the ARCHITECT Active-B12 (Holotranscobalamin). A summary of the non-clinical performance data included in this 510(k) submission has been presented.

Dilution Linearity

The Axis-Shield Active-B12 (Holotranscobalamin) EIA demonstrated linearity across the measuring range of the assay from 5.3 to 156.0 pmol/L.

Reportable Range

The Axis-Shield Active-B12 (Holotranscobalamin) EIA reportable range is 10 to 128 pmol/L.

Analytical limits at low levels

In a representative study, the limit of blank of the Axis-Shield Active-B12 (Holotranscobalamin) EIA was 4.9 pmol/L, the limit of detection was 8.1 pmol/L and the limit of quantification was 8.3 pmol/L.

High Dose Hook

No high dose hook effect was detected up to a concentration of 2236pmol/L Holotranscobalamin.

Cross-reactivity

The Axis-Shield Active-B12 (Holotranscobalamin) EIA is designed to have a maximum deviation in holotranscobalamin concentration of ≤10% in the presence of 500 pmol/L apotranscobalamin or 5000 pmol/L haptocorrin. The maximum deviation in holotranscobalamin concentration ranged from -5% to 1%.

Interference

The Axis-Shield Active-B12 (Holotranscobalamin) EIA is designed to have a maximum deviation in holotranscobalamin concentration of ≤10% in the presence of potentially interfering compounds. The maximum deviation in holotranscobalamin concentration ranged from –10% to 8% for the potentially interfering compounds presented.

Potential Interfering Substance	No interference found up to the following concentration
Haemoglobin	500 mg/dL
Bilirubin	30 mg/dL
Triglyceride (Intralipid Solution)	3000 mg/dL
Rheumatoid Factor	7500 IU/dL
Total Protein	9000 mg/dL

Precision

8 human serum samples were assayed using 3 lots of reagents. Samples were assayed by 2 operators in replicates of 8, once a day for 5 days (total n=80). Data from this study are summarised in the following table:

Sample	n	Lot	Operator	Mean (pmol/l)	Intra-assay %CV	Total %CV
1 A	80	1	1	17.8	7.5%	8.2%
			2	17.5	3.1%	9.3%
		2	1	20.1	6.0%	6.6%
			2	20.3	6.9%	9.2%
		3	1	19.1	5.5%	8.0%
			2	18.9	8.5%	11.0%
2 A	80	1	1	21.8	5.5%	9.9%
			2	21.8	3.9%	7.5%
		2	1	22.6	5.6%	8.7%
			2	23.5	9.0%	10.3%
		3	1	23.9	7.0%	10.2%
			2	23.2	5.8%	8.9%
3 A	80	1	1	28.8	3.8%	7.8%
			2	30.7	4.3%	9.6%
		2	1	31.0	6.8%	8.0%
			2	31.4	4.3%	6.1%
		3	1	31.5	4.5%	6.4%
			2	32.2	4.0%	9.2%
4 A	80	1	1	49.3	3.9%	7.4%
			2	52.6	4.1%	6.7%
		2	1	50.8	5.6%	10.0%
			2	51.7	4.7%	5.9%
		3	1	52.6	4.6%	4.8%
			2	55.0	5.5%	6.1%
5 A	80	1	1	68.4	4.0%	7.6%
			2	73.2	3.7%	7.5%
		2	1	74.8	4.3%	8.2%
			2	75.9	4.6%	6.4%
		3	1	75.1	4.4%	7.9%
			2	76.3	4.9%	6.2%
7 A	80	1	1	115.9	4.2%	5.9%
			2	121.1	3.6%	7.0%
		2	1	123.2	4.3%	10.2%
			2	124.0	4.2%	6.4%
		3	1	127.0	4.8%	10.1%
			2	129.5	3.2%	5.6%
Low Control	80	1	1	23.7	9.4%	10.9%
			2	23.8	5.1%	11.5%
		2	1	20.0	6.0%	7.5%
			2	18.6	5.8%	8.5%
		3	1	20.3	8.3%	9.7%
			2	20.1	8.3%	10.0%
High Control	80	1	1	61.2	6.3%	6.4%
			2	58.8	4.5%	8.9%
		2	1	50.3	6.3%	8.1%
			2	50.2	5.9%	8.4%
		3	1	52.2	7.7%	9.2%
			2	50.8	5.8%	8.5%

Matrix Comparison

Specimens collected in serum (clot) and serum separator (SST) tubes are compatible in the Axis-Shield Active-B12 (Holotranscobalamin) assay shown by a correlation study. The data obtained gave the following statistical values:

Axis-Shield Active-B12 (Holotranscobalamin) EIA – Serum clot versus Serum Separator	
Number of Specimens (n)	> 36
Slope of regression line (Passing-Bablok regression)	> 0.97
Correlation coefficient (r) (Pearson)	0.98
Overall percent bias (%)	< 2.5

Summary of Clinical Performance:

The Axis-Shield Active-B12 (Holotranscobalamin) assay demonstrated substantially equivalent clinical performance to the ARCHITECT Active-B12 (Holotranscobalamin) as indicated by a method comparison study.

Method Comparison

A correlation study was performed with serum specimens from apparently healthy adults. All specimens were analysed using the Axis-Shield Active-B12 (Holotranscobalamin) EIA and a commercially available assay for Holotranscobalamin according to the CLSI document EP9-A2. Specimen concentrations ranged from 13.8 to 112.8 pmol/L in the assay. The data obtained gave the following statistical values:

Axis-Shield Active-B12 (Holotranscobalamin) EIA versus a commercially available assay	
Number of specimens	111
Slope of regression line (Passing-Bablok regression) (95% CI)	0.95 (0.89 to 1.01)
Y-intercept (Passing-Bablok regression) (95% CI)	8.39 (5.73 to 11.77)
Correlation coefficient (r) (Pearson) (95% CI)	0.93 (0.90 to 0.95)

Conclusion:

Based on the performance characteristics the Axis-Shield Active-B12 (Holotranscobalamin) assay (K121946) is substantially equivalent to the predicate device.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

March 22, 2013

Axis-Shield Diagnostics, Ltd.
c/o Simon J. Richards, PhD
The Technology Park, Luna Place
Dundee, Scotland
United Kingdom, DD2 1XA

Re: k121946
Trade/Device Name: Axis-Shield Active-B12 (Holotranscobalamin)
Regulation Number: 21 CFR 862.1810
Regulation Name: Vitamin B_{12} test system
Regulatory Class: Class II
Product Code: CDD
Dated: February 08, 2013
Received: February 11, 2013

Dear Dr. Richards:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Carol C. Benson -S for

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indication for Use

510(k) Number (if known): k121946

Device Name: Axis-Shield Active-B12 (Holotranscobalamin)

Indication For Use:

The Axis-Shield Active-B12 (Holotranscobalamin) assay is an enzyme-immunoassay (EIA) for the quantitative determination of holotranscobalamin (HoloTC) in human serum. HoloTC (vitamin B_{12} bound to transcobalamin) is used as an aid in the diagnosis and treatment of vitamin B_{12} deficiency.

For in vitro diagnostic use.

Prescription Use __X____ (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostics and Radiological Health (OIR)

Yung W. Chan -S

Division Sign-Off
Office of In Vitro Diagnostics and Radiological Health

510(k)__k121946____